IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Kasid et al.

Application No. 10/075,994

Filed: February 15, 2002

Group Art Unit: Unassigned

Examiner: Unassigned

For: LIPOSOMES CONTAINING OLIGONUCLEOTIDES

INDICATION OF CHANGES MADE TO THE SPECIFICATION UPON ENTRY OF THE AMENDMENT SUBMITTED ON JANUARY 24, 2003

The following indicates amendments made to paragraphs at pages 5, 18, and 30 of the specification. Deleted text appears in brackets, added text appears in underlining and with highliting, as portions of the text not amended herein already are intended to be underlined

Amendments to the paragraph bridging lines 12-19 of page 5:

It is an even more specific object of the invention to administer oligonucleotides comprising 5'-GTG-CTCCATTGATGC-3' (SEQ ID NO:1) and/or 5'-CCTGTATGTGCTCCATT-GATGCAGC-3' (SEQ ID NO:2), preferably encapsulated in a cationic liposome, wherein the bases of said oligonucleotides may be modified or unmodified, as an adjunct to chemotherapy. It is another specific object of the invention to chemosensitize tumor tissue to chemotherapeutic agent(s) by the administration of a cationic liposome containing at least one oligonucleotide, preferably an anti-sense oligonucleotide corresponding to a surface or internal antigen or oncogene expressed by the tumor, prior, concurrent or after administration of the chemotherapeutic.

Amendments to the paragraph bridging lines 11-20 of page 18:

Oligodeoxyribonucleotide sequences directed toward the translation initiation site of human c-[rnf] raf-1 cDNA were synthesized at [L of strand] Lofstrand Labs Limited (Gaithersburg, MD, USA) using beta-cyanoethyl phosphoramide chemistry on a Biosearch 8450 DNA synthesizer. The sense (ATG-S) and antisense (ATG-AS) raf ODN sequences were g'-GCAT-CAATGGAGCAC-3' (SEQ ID NO:3) and 5'-GTG-CTCCATTGATGC-3' (SEQ ID NO:4), respectively. One terminal base linkage at each end was modified to a phosphoramide group using 3H-1, 2-benzo-dithiole-3-1, 1,1-dioxide as the sulferizing agent.

Oligos were synthesized at the 15 μm scale and purified on reverse phase chromatography columns. For quality control, a small aliquot of each oligo preparation was ^{32}P-end-labeled and visualized by polyacrylamide gel electrophoresis (20% acrylamide and 5% bis) followed by densitometric scanning of the labeled products.

Amendments to the paragraph bridging lines 22-28 of page 30:

A 20-mer phosphorothioate antisense ODN (ISIS 5132/5132: 5'-TCC-CGC-CTG-TGA-CAT-GCA-TT-3' (SEQ ID NO:4) corresponding to the 3' untranslated region (3'-UTR) of human c-raf-1 mRNA and a seven base mismatched phosphorothioate antisense ODN (SS 10353/10353; 5'-TCC-CGC-GCA-CTT-GAT-GCA-TT-3' (SEQ ID NO:5) were designed and synthesized as described previously (Monia et al., 1996a,b). A 20-mer phosphorothioate sense ODN (5'-ATT-GCA-TGT-CAC-AGG-CGG-GA-3' (SEQ ID NO:6)) was synthesized at Loftstrand Labs Limited (Gaithersburg, MD) as described previously (Soldatenkov et al., 1997)